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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,070	05/11/2006	Hoon Han	36470-231114	3303

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VENABLE LLP
P.O. BOX 34385
WASHINGTON, DC 20043-9998

EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
04/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,070	HAN ET AL.	
	Examiner	Art Unit	
	FEREYDOUN G. SAJJADI	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/11/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3 are pending in the Application, and are under current examination.

Information Disclosure Statement

The information disclosure statement dated 12/31/2007 has been considered and indicated as such on Form PTO-SB/08A.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 are rejected under 35 U.S.C. §103(a) as being unpatentable over Erices et al. (Br. J. Hematol. 109:235-242; 2000), in view of Nishikawa et al. (U.S. Patent Application Publication No.: 2004/0235160; effective filing date: Aug. 7, 2002), and further in view of Petaja et al. (J. Clin. Invest. 99:2655-2663; 1997).

The claims embrace a method for isolating and culturing mesenchymal stem cells from umbilical cord blood comprising obtaining umbilical cord blood within 24 hours post partum, adding an anti-coagulant to said blood at more than 45 ml per unit, diluting the resulting mixture 2-fold with α-MEM medium, centrifuging over Ficoll-Hypaque to harvest monocytes, and subjecting the monocytes to α-MEM medium containing glutamine, fetal bovine serum, an antibiotic, an anti-fungal agent, stem cell factor (SCF), granulocyte macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (G-CSF), interleukin-3 (IL-

3) and interleukin-6 (IL-6). It is noted that the reference to the concentration of anti-coagulant as more than 45 ml per unit is unconventional, given that the art-recognized nomenclature for anti-coagulants such as heparin is units per ml. The instantly claimed concentration, when given its most reasonable interpretation would be equivalent to less than 0.02U/ml.

Erices et al. describe the harvest and preparation of mesenchymal progenitor cells from human umbilical cord blood (Title and Abstract). Specifically describing the harvest of cord blood from preterm and term deliveries by processing blood samples ≤ 24 hours after harvest, wherein the cord blood was drained into glass bottles containing 10 ml of M-199 culture medium containing heparin (an anti-coagulant). The diluted cord blood cells are further described as separated into low-density fraction on Hystopaque-1077® (Sigma; functional equivalent of Ficoll-Hypaque (Pharmacia); both having a specific gravity of 1.077 g/ml), to obtain mononuclear cells (i.e. monocytes), that were suspended into culture medium comprising α-MEM, fetal bovine serum and gentamycin sulfate (second column, p. 235 to second column, p. 236). The characterization of adherent primary culture mesenchymal cells are described in the second column, p. 238.

It should be noted that the fold-dilution of cord blood with medium, prior to gradient centrifugation can vary depending upon the volume of cord blood obtained and the volume of Ficoll-Hypaque to be centrifuged. Moreover, the medium for dilution of the cells prior to centrifugation may be M-199 or α-MEM, both disclosed by Erices et al.; that a person of ordinary skill in the art would regard as functional equivalents for the purposes of dilution. Thus, the limitation of 2-fold dilution is obvious due to the requirements of the Ficoll-Hypaque density gradient.

While Erices et al. do not describe the inclusion of glutamine, cytokine growth factors or anti-fungal agent in their culture medium, the inclusion of such factors as a cocktail for mesenchymal cell culture was well known in the prior art.

Nishikawa et al. describe methods for culturing human mesenchymal stem cells and hematopoietic stem cells (Example 5, p. 8), including the isolation of human umbilical cord blood stem cells following the separation of mononuclear cells by density gradient centrifugation

of heparinised umbilical cord blood overlaid on Ficoll-paque (Example 6, p. 8). Nishikawa et al. describe conditions for cell growth in medium supplemented with L-glutamine, antibiotics, amphotericin B (an antimicotic), SCF, G-CSF, IL-3 and IL-6 (¶ [0076], p. 9), that may additionally include GM-CSF (¶ [0032], p. 3); thus curing the deficiency of mesenchymal cell culture supplements in Erices et al.

While neither Erices et al. nor Nishikawa et al. disclose the addition of heparin to the umbilical cord blood at a concentration of less than 0.02 U/ml, the effectiveness of heparin as an anti-coagulant at low concentration was known in the prior art.

Petaja et al. in studying the mechanism of anticoagulant action of heparin, observed that the addition of 0.016 U/ml of heparin to plasma rendered the plasma unclottable (second column, p. 2661; Figs. 1 and 2); thus providing the motivation to employ low concentrations of heparin as an anticoagulant. Applicants should further note that as indicated in MPEP 2144.05: Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

As the methods described by Erices et al. and Nishikawa et al. are directed to the isolation of monocytes from heparinised umbilical cord blood for culture and production of mesenchymal stem cells, it would have been *prima facie* obvious for one of ordinary skill in the art at the time of the instant invention to combine their respective teachings to include the culture supplements of Nishikawa et al., and to further utilize a low heparin concentration as described by Petaja et al., in the method of Erices et all, thus resulting in the method of instantly claimed invention. Therefore, an artisan of ordinary skill, having combined the elements of low heparin concentration and various mesenchymal cell culture supplements in the monocyte isolation and culture method of Erices et al. would have a reasonable expectation of success in producing mesenchymal stem cells via instantly claimed method of isolating and culturing monocytes.

Conclusion

Claims 1-3 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/

Fereydoun G. Sajjadi, Ph.D.
Examiner, Art Unit 1633